Figure 1. Spectrum of morphology in sclerotic cGVHD. A: Lichen sclerosus like disease with profound dyspigmentation in patient 3. B: Myofascial disease in patient 9. C: Penile lichen sclerosus in patient 7. D. Dermal sclerotic plaques with "choke-hold" distribution in Patient 4. E and F: Bound down sclerosis of toes and guttate sclerotic papules and plaques in patient 8.

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Eosinophilia, Edema, and Nail Dystrophy: Harbingers of Severe Chronic Graft Versus Host Disease of the Skin in Children

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Skin involvement has been shown to be predictive of poor prognosis in patients with chronic graft-versus-host disease (cGVHD). However, cGVHD of the skin has not been well described in children. The purpose of this study was to characterize distribution, type, and extent of skin cGVHD and correlate findings with laboratory markers, severity of disease, and multi-organ involvement in a cohort of pediatric hematopoietic stem cell transplant recipients. 12 consecutive pediatric patients with skin cGVHD seen at Dana-Farber Cancer Institute and Boston Children's Hospital were evaluated over a 2-year period. 6 (50%) patients had de novo, 4 had progressive, and 2 had quiescent onset cGVHD. Type of skin GVHD included sclerotic (9), eczematous (2), and ichthyosiform (1). 8 of 9 (89%) patients with sclerotic cGVHD had multi-organ involvement; 1 of 3 (33%) patients with non-sclerotic disease had multi-organ involvement. All patients with sclerotic cGVHD had steroid resistant disease while all patients with non-sclerotic cGVHD responded either to topical therapy or prednisone alone. Peripheral eosinophil counts $>$ 300 cells/uL was identified in 10 patients prior to onset of cGVHD, of whom only one could be attributed to drug hypersensitivity. Mean peak peripheral eosinophil count of those with myofascial sclerotic cGVHD was significantly higher than that of remaining patients (1962 cells/uL vs. 525 cells/uL, p=0.03). Mean time of onset of eosinophilia for patients with myofascial sclerotic cGVHD was 79 days (range 21-182) prior to onset of cGVHD. 6 patients were noted to have otherwise unexplained edema of the

Figure 2. Preceding edema was noted in 6 of 9 patients with sclerotic cGVHD. Clockwise from left upper: Patient 9,9,7.

Figure 3. Ptyerygium inversum unguis in 4 participants with severe cGVHD characterized by sclerotic involvement and lung disease. Clockwise from left upper: Patient 7, 3, 4, 12.

lower ± upper limbs prior to onset of skin cGVHD. Patients with myofascial sclerotic cGVHD were significantly more likely than those with other types of skin cGVHD to have preceding peripheral edema (6/6 vs. 0/4, p=0.005). In addition, patients with severe cGVHD were significantly more likely than those with mild or moderate cGVHD to have preceding peripheral edema (5/5 vs. 1/5, p=0.05). Nail dystrophy was present in 7/12 (58%) patients in our cohort, and was significantly more likely to occur in patients with myofascial sclerotic cGVHD than those with other forms of skin cGVHD (7/7 vs. 1/5, p=0.01). Pterygium inversum inguis, a specific form of nail dystrophy, was present in 4 of 12 patients, and was significantly more likely to occur in patients awaiting lung transplantation (3/4 vs. 0/8, p=0.02). This study represents the largest cohort of pediatric patients with skin cGVHD reported in the literature and suggests that peripheral eosinophilia, edema, and nail dystrophy are harbingers of severe cGVHD of the skin in children.

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Changes in Red Blood Cell Mean Corpuscular Volume after Pediatric HSCT

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Background: While it has been noted clinically that the mean corpuscular volume (MCV) for HSCT recipients may tend to increase over time, literature describing changes to mean corpuscular volume (MCV) following pediatric HSCT is very limited. Macrocytosis is of clinical interest because it may signal underlying bone marrow dysfunction. Consequently, understanding the natural course of changes in the MCV over time is important.

Methods: We conducted a retrospective chart review of all pediatric patients undergoing allogeneic (allo) or autologous (auto) HSCT at the Medical University of South Carolina during July 1, 2007-June 30, 2012 who have survived for >1 year after transplant without relapse. The sample included 16 auto-HSCT patients (10 patients with incomplete data) and 32 allo-HSCT patients. Baseline MCV values were recorded both at baseline (PBSC collection date for auto patients, HSCT admission date for allo patients) and at specific intervals post-HSCT. Data was analyzed to identify the presence of macrocytosis based on age-specific normal values, the trend of MCV changes with time, and the time of maximum change in MCV. Linear regression was used to evaluate associations between factors and MCV changes. Statistical significance was accepted at $P<0.05$.

Results: Macrocytosis was present at baseline in 19% of the allo patients and 0% of the auto patients. Maximum mean MCV change for allo and auto patients was at 90 days post-HSCT. At day 90, allo patients had a mean increase in MCV of 5.77 fl (95% CI 2.77- 8.77), and auto patients had a mean increase in MCV of 8.33 fl (95% CI 2.80-13.87). For allo patients, 56%, 32%, and 40% were macrocytic at days 90, 365, and 730 post-HSCT. For auto patients, 67%, 40%, and 40% were macrocytic at days 90, 365, and 730 post-HSCT. For allo patients, MCV changes were associated with ABO incompatibility (p=0.043) but not with age, sex, diagnosis, disease status at HSCT, prep regimen, graft source, cell dose, GVHD, neutrophil engraftment, or platelet engraftment. Compared to patients with no ABO incompatibility, the mean change in MCV at day 90 was 14.38 fl less for patients with minor ABO incompatibility but was not significantly different for patients with major ABO incompatibility. For auto patients, MCV changes had a positive association with neutrophil engraftment (p=0.049) with a trend towards an association with cell dose (p=0.071) but not with age, sex, diagnosis, initial chemotherapy, disease status at HSCT, prep regimen, or platelet engraftment. For each additional day increase in neutrophil engraftment, the mean change in MCV at day 90 is expected to increase by 1.91 fl.